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CASE REPORT

Serious envenomation after a snakebite by a Western bush viper *(Atheris chlorechis)* in the Netherlands: a case report

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ABSTRACT

Venomous snakebites are a rarity in the Netherlands. In this report we describe the case of a 26-year-old male amateur snakekeeper who was bitten in his left index finger by a Western bush viper (*Atheris chlorechis*). His clinical condition deteriorated rapidly with acute renal failure and considerable blood loss due to coagulopathy. Antidote was not readily available and was finally supplied by a zoo in Antwerp, Belgium. One day after admission the blood loss diminished.

KEYWORDS

Antidote, *Atheris chlorechis,* bites, coagulopathy, F(ab), renal failure, venomous snake

INTRODUCTION

In the Netherlands, snakebites are rarely seen. The only natural occurring venomous snake is the *Vipera berus*, which seldom bites humans. We present the case of a patient who developed severe coagulopathy, anaemia and acute renal failure after a bite by a Western bush viper.

CASE REPORT

A 26-year-old man was admitted to hospital after being bitten in his left index finger while feeding his pet snake, a Western bush viper (*Atheris chlorechis*). One year earlier he had been admitted to the same hospital for observation after a bite by a *Gila monster*, a venomous lizard. There was no other relevant medical history and he was not taking any medication.

The patient arrived at hospital immediately after being bitten. He remained calm and had not applied any bandages to the bite wound. His distal left index finger was swollen and very painful. There were no other symptoms and physical examination did not reveal any abnormalities. Laboratory examination showed a slight thrombocytopenia (128 x 10^9/l). Because of a developing compartment syndrome, fasciotomy of the distal phalanx was performed after which the patient was admitted to the general ward for observation.

Seven hours after the bite, the pain increased while the swelling had progressed to his wrist. Also, the patient became dizzy. Laboratory research revealed severe coagulopathy and worsening of renal function (*table 1*). It was decided to give an antidote. Since it was not available in the Netherlands, it had to be sent for from Belgium (zoo in Antwerp, 300 km). In the mean time he was taken to the operating theatre for a second fasciotomy. The finger was now opened from the distal to proximal phalanx under general anaesthesia, while fresh frozen plasma (FFP) was given in order to optimise coagulation. After this procedure, he was admitted to our intensive care unit.

The patient was sedated and remained intubated. His left hand was packed with a pressure bandage, out of which blood was continuously leaking. A nasogastric tube yielded blood and coffee-ground material. He had been anuric since ICU admission. Further physical examination did not reveal any abnormalities. Laboratory results are shown in *table 1*. Due to treatment with FFP during surgery the activated partial thromboplastin time (APTT) and prothrombin time (PT) had normalised. Nonetheless, massive bleeding continued and worsened. In the first six hours on the ICU the patient lost approximately five litres of blood. More FFP and thrombocyte-concentrate were given. The antidote (FAV AFRIQUE, Aventis Pasteur, France)

arrived 12 hours after the bite. First, a small amount of antidote was given subcutaneously. No adverse reactions were seen within half an hour. Then two 10 cc vials of antidote were diluted in 500 cc saline 0.9% and given intravenously in two hours. This was repeated twice. Red blood cells, crystalloids and vasopressors were additionally started to keep a systolic blood pressure above 80 mmHg. The blood loss slowly diminished in the following hours. The wound and insertion sites of lines kept leaking for up to four days. On the second day in the ICU sedatives were stopped and he was successfully extubated. His neurological function was normal. Anaemia persisted in combination with an elevated lactate dehydrogenase (LDH) (*table 2*), suggesting haemolysis. Unfortunately no other laboratory parameters proving haemolysis are available. Because of anuria he required haemodialysis. Six days after admission to the ICU the patient could be transferred to the general ward. After two weeks the number of platelets normalised (*table 2*) and in the third week renal function returned to normal. The finger healed well except for a small necrotic area at the distal phalanx.

DISCUSSION

In this case report we describe the consequences of a bite by an *Atheris chlorechis* and will discuss the treatment of this patient step by step. The *Atheris chlorechis* is similar to the pit viper, a member of the family *Viperidae*, one of the venomous snake families. Not every bite by a venomous snake results in envenomation. For example, of all pit viper bites, 25% do not result in envenomation and another 15% are so trivial that they only require local cleansing and tetanus prophylaxis.[1]

Table 1. *Laboratory results on the first day after a snake bite*

	Admission	+5.5 hours	+11.5 hours (admission ICU)	+14 hours	+17.5 hours
Leucocytes (4.0-10.0 10^9/l)	3.3	9.5	5.9	4.5	6.3
Haemoglobin (8.7-10.6 mmol/l)	9.4	8.7	6.1	4.0	5.8
Haematocrit (0.420-0.520v/v)	0.434	0.398	0.272	0.180	0.270
Platelets (150-350 10^9/l)	128	83	56	59	43
Sodium (132-144 mmol/l)	142	141	141	142	140
Potassium (3.6-4.8 mmol/l)	4.1	4.0	5.0	3.9	4.8
Urea (3.3-6.7 mmol/l)	8.5	12.6	15.1	16.2	17.2
Creatinine (62-106 umol/l)	108	206	268	292	314
LDH (114-235 U/l)	267	1458	1266	1050	982
ASAT (0-40 U/l)	23	71	73	64	73
ALAT (0-30 U/l)	28	30	32	44	51
Total bilirubins (3-26 µmol/l)	10	76	58	51	42
Direct bilirubins (0-5 µmol/l)	6	30	19	16	14
PT (11-16 sec)	13.3	>120	17.0	16.9	15.7
APTT (26-36 sec)	28.1	>200	40.6	39.2	34.8
Fibrinogen (1.7-3.5 g/l)	2.0	0.7	0.6	0.9	1.1
Antithrombin (75-125%)	102	105	106	NA	NA

During the first 14 hours FFP and thrombocyte-concentrate were given. NA = not available. LDH = lactate dehydrogenase; ASAT = aspartate aminotransferase; ALAT = alanine aminotransferase; PT = prothrombin time; APTT = activated partial thromboplastin time.

Table 2. *Laboratory results follow-up during ICU stay*

	Day 1			Day 2	Day 3	Day 4	Day 5	Day 6
Haemoglobin (8.7-10.6 mmol/l)	9.4	8.7	4.0	3.9	3.7	4.1	4.3	3.7
Platelets (150-350 10^9/l)	128	83	59	35	24	22	19	34
LDH (114-235 U/l)	267	1458	1050	2217	3761	5144	5750	3561
PT (11-16 sec)	13.3	>120	16.9	13.5	13.3	13.6	13.0	NA
APTT (26-36 sec)	28.1	>200	39.2	29.4	30.6	33.2	29.8	NA
Fibrinogen (1.7-3.5 g/l)	2.0	0.7	0.9	1.0	1.4	NA	2.1	NA
Antithrombin (75-125%)	102	105	NA	114	NA	NA	112	NA

NA = not available. LDH = lactate dehydrogenase; PT = prothrombin time; APTT = activated partial thromboplastin time.

Snake venom is a chemically complex mixture of water, enzymes and a large number of peptides. The venom has two purposes. The first is killing the prey and the second is digesting the prey as early as possible. Injecting the digestive enzymes is more effective than digesting from the outside, especially if the prey is swallowed whole without chewing. The composition of venom varies with the species and age of the snake. The various proteins and peptides induce endothelial damage by causing blebs, dilating the perinuclear space, and breakdown of the plasma membrane with accumulation of extravascular fluids and cells. The digestive enzymes in snake venom cause both local and systemic damage to human tissue. At least 26 different digestive enzymes have been identified although no single snake venom contains all of them. Among the enzymes are:

- Phospholipases, which damage the fatty acid phospholipid fraction of cell membranes. In red blood cells this and other factors contribute to the development of intravascular haemolysis;
- Hyaluronidase, which decreases the viscosity of connective tissue to allow venom spread beyond the bite site;
- Proteolytic enzymes such as R-Nase, D-Nase, and 5' nucleotidase are present that can damage muscle fibre proteins;[2]
- Amino acid esterase and other thrombin-like enzymes that promote fibrin formation resulting in a consumptive coagulopathy with prolonged clotting times and hypofibrinogenaemia.

Other manifestations of coagulopathy and causes of bleeding after a snake bite are: a) reduced coagulability of blood, anticoagulant effect of the venom, b) direct damage to blood vessels, c) diminished platelet function and d) secondary effects due to shock.

As a general rule, field management after a snakebite involves keeping the patient calm and seeking help immediately.[3] The patient knew the type of snake he was bitten by and did not apply a tourniquet. Viper venom primarily produces local necrosis and localisation of toxin may in fact worsen the syndrome. In the emergency room and on the general ward, it was decided to perform a fasciotomy because the patient developed signs of compartment syndrome. The repeated fasciotomy in combination with the developing coagulopathy resulted in life-threatening blood loss. The evidence of a surgical approach is sparse as Hall discussed in surgical intervention in *Crotaline* snake envenomation.[4] The *Crotaline* species also belongs to the viper family, as does the *Atheris* species. Their venom mimics signs and symptoms of compartment syndrome closely. True compartment syndrome is thought to occur rarely and the presenting signs are caused by myonecrosis related to the action of the venom components rather than to elevated compartment pressure that causes vascular insufficiency. We feel that in our case manipulation to the bite site may have contributed to the clinical deterioration.

The renal failure in snakebites may be the result of a combination of intravascular haemolysis, a syndrome resembling disseminated intravascular coagulation, hypotension or nephrotoxic effects of components of venom. In our patient, because of adequate resuscitation and intensive care facilities, no hypotension was observed. During surgery FFP and thrombocyte concentrate were given to temporarily restore blood coagulability as assessed by prolonged PT and APTT. On admission to the ICU bleeding at the site of the bite, from venipuncture sites, gums and stomach indicated recurrence of incoagulable blood. Since the swelling was progressive with clinical deterioration we decided to give antivenom. Although prospective randomised controlled trials are lacking in the literature some suggest that antivenom immunotherapy is the only effective treatment against severe envenomations.[5,6]

Traditionally, horse serum preparations were used that often produced immediate and late-onset hypersensitivity reactions. Recently, new antivenoms based on the antigen-binding fragments of immunoglobulines (F(ab fragments)) have been produced. FAV AFRIQUE is a polyvalent antivenom made from fragments of IgG, $F(ab')_2$, whose manufacturing process involves several additional purification steps compared with those classically used. Theoretically, Fab_2 fragments do not induce the formation of immune complexes and thus carry less risk in severe antivenom reactions.[7] Chippaux *et al.* demonstrated in an uncontrolled study the favourable safety and efficacy profile of FAV AFRIQUE.[8] FAV AFRIQUE is indicated for the treatment of envenomation caused by most venomous snakes found in Africa. No specific antivenom exists for the *Atheris chlorechis* venom. Twelve hours after the bite the antidote became available for our patient. To prevent early anaphylactoid reactions prednisolone and antihistamine were given intravenously.[9] After administration of six vials of antidote in six hours, cessation of bleeding was achieved. Possible haemolytic anaemia, as indicated by elevated LDH, remained for several days.

In any patient with a coagulopathy the most important aspect of management is the recognition of the underlying disease and removal of the initiating factors. If specific therapy and support is successful and for instance disseminated intravascular coagulation is reversed no replacement therapy is required. Snakebite-induced coagulopathy is not entirely like other forms of coagulopathy. It may present with severe disturbance of laboratory values but in contrast to other diseases this does not equate to actual morbidity in an individual patient.

Experience from personal communications, anecdotal reports, books and reviews[10] has led to the consensus that:

- Antivenom is the treatment of choice for haemostatic failure as an attempt to eliminate the cause of the disease;
- Applying standard wound care protocols or replacement therapy for coagulopathy (e.g. FFP) can be dangerous and may add fuel to the fire with acceleration of fibrinolysis and increased risk of bleeding.[10]

In conclusion, we present a patient in the Netherlands with massive bleeding and acute renal failure due to snake envenomation. We feel that early surgical manipulation to the bite site worsened the local bleeding and failed to prevent remote organ dysfunction and may actually be considered to be harmful and highly controversial. Severe blood loss stopped after treatment with blood products and antivenom. It is tempting but it cannot be concluded from our data that venom neutralisation by FAV AFRIQUE is the major component in treating systemic bleeding and restoring blood coagulability.

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